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EXAMINER

KERR, KATHLEEN M

| ART UNIT | PAPER NUMBER |
|----------|--------------|
|----------|--------------|

1652

DATE MAILED: 05/03/2002

24

Please find below and/or attached an Office communication concerning this application or proceeding.

# Office Action Summary

Application No.

09/311,689

Applicant(s)

RAO ET AL.

Examiner

Kathleen M Kerr

Art Unit

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

## Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☒ Responsive to communication(s) filed on 26 February 2002.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 9-25, 28-32, 54-87, 96 and 97 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 10, 11, 13, 15-17, 20, 56 and 96 is/are allowed.
- 6) ☒ Claim(s) 9, 12, 14, 18, 19, 21, 28-32 and 57-87 is/are rejected.
- 7) ☒ Claim(s) 22-25, 54, 55 and 97 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☒ The proposed drawing correction filed on 31 December 2001 is: a) ☒ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

## Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

## Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 18.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other:

## **DETAILED ACTION**

### ***Application Status***

1. In response to the previous Office action (Paper No. 17 mailed May 29, 2001), Applicants filed an amendment and an incomplete response (Paper No. 19 on December 31, 2001) due to a damaged replacement sequence disk. Applicants filed a new disk on February 26, 2002 (Paper No. 21). The combination of Paper Nos. 19 and 21 constitute a complete response to Paper No. 17.

The amendment filed on December 31, 2001 cancelled claims 1-8, 33-47, 49-53, and 88-95, amended Claims 9-14, 16-22, 24, 28-32, 54-56, 59-62, 69, 71-72, 74, 76, 78-87 and added new Claims 96 and 97. Claims 96 and 97 are drawn to the elected invention. Claims 9-25, 28-32, 54-87, 96, and 97 are pending in the instant application and will be examined herein.

### ***Priority***

2. As previously noted, the instant application is granted the benefit of priority of U.S. Application Nos. 08/740,682, filed on November 1, 1996 and 09/297,418, filed on April 30, 1999, which claims priority to PCT/US97/20441 filed on October 31, 1997.

### ***Information Disclosure Statement***

3. The information disclosure statement filed on June 15, 2001 (Paper No. 18) has been reviewed, and its references have been considered as shown by the Examiner's initials on the attached copies.

*Drawings*

4. Applicants' amended drawings (2 sheets) filed on December 31, 2001 have been entered. The amended drawings have been approved by the Draftsmen and are, therefore, entered as formal drawings acceptable for publication upon the identification of allowable subject matter.

*Compliance with the Sequence Rules*

5. The amendments to the drawings and the specification have corrected the errors for the Figures. However, the oligonucleotides on pages 50-54 still have not been identified by SEQ ID NO. Applicants note SEQ ID NOs for these sequences on page 14 of the amendment in the remarks. However, the specification has not been amended to incorporate these changes. Appropriate amendment to the specification is required to bring the instant application into compliance with the sequence rules.

*Withdrawn - Objections to the Specification*

6. Previous objection to the specification for inappropriate notation of an Internet address is withdrawn by virtue of Applicants' amendment.

7. The previous new matter objection against the disclosure (Paper No. 17, item 9) has been withdrawn in part.

- a) Applicants' amendment to Claim 9, 54, and 55 to alter the mole percentages to those described in the specification as originally filed has rendered moot points a-d.
- b) Applicants amendments to Claim 59 from "about 15% or more lysine" to ---more than seven lysine amino acid residues--- and to Claim 60 from "about 20% or more lysine" to

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---more than ten lysine amino acid residues--- are supported by the specification as originally filed and renders this point of item e moot.

- c) Applicants' amendment to Claims 61, 72, 74, and 76 to alter "at 4 to about 34 positions" or "at 6 to about 34 positions" or "at least 23 amino acids in length" to ---more than four non-native essential amino acids--- or ---more than seven non-native essential amino acids--- or ---more than eleven non-native essential amino acids--- has rendered this portion of points g-j moot.
- d) Applicants wholly amended Claims 78-84 and 87 in an attempt to remove new matter. None of the previously cited new matter remains, and points k-r are moot. However, a new, new matter objection is noted below.

***Maintained - Objections to the Specification***

8. Previous objection to the Abstract for not completely describing the disclosed subject matter is maintained. The Examiner indicated that sources of the protein be amended into the Abstract. Particularly, genus/species of organisms from which the initial polypeptides of the invention were obtained is required.

9. The previous new matter objection against the disclosure (Paper No. 17, item 9) has been maintained in part. Explanation concerning the individual items are noted below.

- a) Applicants argue that in Claim 59 (e), the phrase "at least 60% sequence identity ...SEQ ID NO:2" is supported by the disclosure in the specification on page 12 referring to "the modified protein". The Examiner finds no definition of "the modified protein" being exactly SEQ ID NO:2. The new matter objection is maintained.

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- b) The objection as new matter in Claims 61, 72, 74, and 76 to references to SEQ ID NO:2, positions 19-83, 19-53 and 63-83 has been traversed. Applicants argue that the ranges cited "19-53 and 70-83", "19-83", in Claims 61, 72, 74, and 76, is supported by various embodiments in the specification, specifically a negative embodiment wherein changes are *not* made at positions 1-18 and 54-69. As noted above, specific embodiments cannot support the genus claimed. Moreover, this negation of alterations in certain segments does not support the positive statement to make modification in the unnamed segments as claimed by Applicants. Therefore, the Examiner maintains the new matter objection in (g-j) in part.

Applicants are required to cancel the new matter in the reply to this Office Action or to point out **precisely** (page and line number) where in the instant application, or where in any incorporated-by-reference publications, clear support for the amendments can be found.

***Withdrawn - Objections to the Claims***

10. Previous objection to Claims 54-55 under 37 C.F.R. § 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim is withdrawn by virtue of Applicants' amendment to Claim 9, the parent claim.

***Withdrawn - Claim Rejections - 35 U.S.C. § 112, second paragraph***

11. Previous rejection of Claims 9-20 and 54-89 under 35 U.S.C. § 112, second paragraph, as being indefinite for the persistent use of confusing numerals is withdrawn by virtue of Applicants' amendment.

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12. Previous rejection of Claims 9 and 54-55 under 35 U.S.C. § 112, second paragraph, as being indefinite for the phrase "composition...or in combinations thereof" is withdrawn by virtue of Applicants' amendment.

13. Previous rejection of Claims 9, 54, 55, 59, and 60 under 35 U.S.C. § 112, second paragraph, as being indefinite for the limiting concept of "mole %" is withdrawn by virtue of Applicants' amendment.

14. Previous rejection of Claims 10-18 and 56 under 35 U.S.C. § 112, second paragraph, as being indefinite for the confusing residues positions as related to SEQ ID NO:4 is withdrawn by virtue of Applicants' amendment.

15. Previous rejection of Claims 10-18, 56, and 61-71 under 35 U.S.C. § 112, second paragraph, as being indefinite for the phrase "modified to contain" is withdrawn by virtue of Applicant's arguments and the Examiner's reconsideration.

16. Previous rejection of Claims 10-25, 56, and 61-86 under 35 U.S.C. § 112, second paragraph, as being indefinite for the phrase "corresponding to" or "correspond to" is withdrawn by virtue of Applicants' arguments and the Examiner's reconsideration.

17. Previous rejection of Claim 11 under 35 U.S.C. § 112, second paragraph, as being indefinite for the phrase conservative substitutions is withdrawn by virtue of Applicants' amendment removing said phrase from the claim.

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18. Previous rejection of Claim 12 under 35 U.S.C. § 112, second paragraph, as being indefinite for the term "reduced" is withdrawn by virtue of Applicants' amendment. However, the polypeptide used to test relative activity, as noted in the amended claim, is unclear. See new 112, second paragraph rejection below.

19. Previous rejection of Claims 13, 14, and 16 under 35 U.S.C. § 112, second paragraph, as being indefinite for the antecedent basis of the term "protein" is withdrawn by virtue of Applicants' amendment.

20. Previous rejection of Claim 13 under 35 U.S.C. § 112, second paragraph, as being indefinite for the term "comprising" is withdrawn by virtue of Applicants' amendment.

21. Previous rejection of Claim 14 under 35 U.S.C. § 112, second paragraph, as being indefinite for) the further comprising language and the brackets is withdrawn by virtue of Applicants' amendment.

22. Previous rejection of Claims 15-18 and 65-66 under 35 U.S.C. § 112, second paragraph, as being indefinite for several phrases is withdrawn by virtue of Applicants' amendment. The only concept that remains unclear, in view of Applicants' amendment, is drawn to residues 1 to 18 of SEQ ID NOs: 2 or 12. A new 112, second paragraph rejection is set forth below to address the amended claim.



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23. Previous rejection of Claims 17, 19-25, 28, 32, and 87 under 35 U.S.C. § 112, second paragraph, as being indefinite for the phrases "Cl-2 like" or "Cl-2 derived" or "homologous to Cl-2" is withdrawn by virtue of Applicants' amendment.

24. Previous rejection of Claims 19-25 under 35 U.S.C. 112, second paragraph, as being indefinite for the particular modification of A75K or T is withdrawn by virtue of Applicants' amendment.

25. Previous rejection of Claims 19-25 under 35 U.S.C. § 112, second paragraph, as being indefinite for the Markush groups in Claim 19 and Claim 21 is withdrawn by virtue of Applicants' amendment.

26. Previous rejection of Claim 20 under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to recite "further comprise" is withdrawn by virtue of Applicants' amendment.

27. Previous rejection of Claim 24 under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to recite "further comprising" is withdrawn by virtue of Applicant's amendment.

28. Previous rejection of Claim 25 under 35 U.S.C. § 112, second paragraph, as being indefinite for the term enriched is withdrawn by virtue of the Examiner's reconsideration in view of Applicants' arguments.

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29. Previous rejection of Claim 28 under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to cite the relative SEQ ID NO is withdrawn by virtue of Applicants' amendment.

30. Previous rejection of Claim 28 under 35 U.S.C. § 112, second paragraph, as being indefinite for the terms "conservatively modified" and "conservatively substituted" is withdrawn by virtue of Applicants' amendment removing said phrases.. Applicants amended the specification to include on "conservatively substituted variants" which, they attest, are limited to the substitutions listed on page 10 of the specification. The Examiner agrees that the instant claims, read in light of the specification, are clear.

31. Previous rejection of Claims 31 and 58 under 35 U.S.C. § 112, second paragraph, as being indefinite for the phrase "wherein the % sequence... Weight of 4" is withdrawn by virtue of Applicants' amendment.

32. Previous rejection of Claim 32 under 35 U.S.C. 112, second paragraph, as being indefinite for the term "immunologically reactive" is withdrawn by virtue of the Examiner's reconsideration in view of Applicant's arguments.

33. Previous rejection of Claim 62 under 35 U.S.C. § 112, second paragraph, as being indefinite for the phrase "a wild-type Cl-2 polypeptide" is withdrawn by virtue of Applicants' amendment.

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34. Previous rejection of Claim 71 under 35 U.S.C. § 112, second paragraph, as being indefinite for the parentheses is withdrawn by virtue of Applicants' amendment.

35. Previous rejection of Claims 78-86 under 35 U.S.C. § 112, second paragraph, as being indefinite for how a 23-mer polypeptide can correspond to positions 19-83 of another sequence is withdrawn by virtue of Applicants' amendment.

36. Previous rejection of Claim 86 under 35 U.S.C. § 112, second paragraph, as being indefinite for the parentheses is withdrawn by virtue of Applicants' amendment.

37. Previous rejection of Claim 88 under 35 U.S.C. § 112, second paragraph, is withdrawn by virtue of Applicants' cancellation of said claim.

***Maintained - Claim Rejections - 35 U.S.C. § 112, second paragraph***

38. Previous rejection of Claims 29 and 62 under 35 U.S.C. § 112, second paragraph, as being indefinite for the terms "conservatively modified" and "conservatively substituted" is maintained. Applicants amended the specification to include on "conservatively substituted variants" which, they attest, are limited to the substitutions listed on page 10 of the specification. However, this citation in the specification is unclear. For example, in the first group of "conservative substitutions", only an arginine can substitute for a lysine; in the second group of "conservative and essential amino acid substitutions", a threonine can substitute for a lysine. Thus, the definition of "conservatively substituted" is unclear.

***Withdrawn - Claim Rejections - 35 U.S.C. § 112, first paragraph***

39. Previous rejection of Claims 9-25, 28, 31, 54-56, 58-61, and 63-86 under 35 U.S.C. § 112, first paragraph, written description, is withdrawn by virtue of Applicants' arguments and amendments and the Examiner's reconsideration. Each of the instant claims contains a definite limit on the structure of the claimed polypeptide by virtue of a percent identity to a disclosed SEQ ID NO. Within this structure, the claimed polypeptides must also have certain criteria related to essential amino acid content. This content provides the "function" of these nutritional supplement polypeptides. In other words, the function is inherent in the structure. Thus, the written description rejection of the instant claims is withdrawn.

40. Previous rejection of Claims 88-89 under 35 U.S.C. § 112, first paragraph, written description, is withdrawn by virtue of Applicants' cancellation of said claims.

41. Previous rejection of Claims 10-25, 28, 32, 56-58, and 61-89 under 35 U.S.C. § 112, first paragraph, scope of enablement, is withdrawn by virtue of Applicants' arguments and the Examiner's reconsideration. Since Applicants describe how to make and use feed additives, and virtually any polypeptide can be used as such, so long as the specification describes how to make the polypeptides, they are also enabled with the function inherently linked to the structure.

***Maintained - Claim Rejections - 35 U.S.C. § 112, first paragraph***

42. Previous rejection of Claims 29, 30, 57, 62 under 35 U.S.C. § 112, first paragraph, written description, is maintained. Applicants' arguments have been considered, but are not deemed persuasive for the following reasons.

Applicants argue that a representative number of species of the claims genus have been described. The Examiner disagrees. The instant claims contain wholly open-ended structural limitation. Unlike the claims (withdrawn rejection) that are bound by an overall percent identity to some SEQ ID NO, the instant claims have no such limitation. Thus, any polypeptide comprising the disclosed sequences is read on. More particularly, for example, a 500 amino acid protein having a particular catalytic activity may fall within the scope of the broad structural claims. The specification describes no such proteins, except that they would make good feed additives. In such a diverse structural group, this position is untenable.

The Examiner suggests the inclusion of a broad structural limitation, such as 30% identity to SEQ ID NO:2. Such a limitation defines the structure so that the inherent function is a real limitation on the claims, although not expressed.

43. Previous rejection of Claim 32 under 35 U.S.C. § 112, first paragraph, written description, is maintained. Applicants' arguments have been fully considered but are not deemed persuasive. Applicants' arguments center on the structure of the claimed polypeptide variants. These arguments are addressed above. The Examiner reiterates the position on the "immunoreactive polypeptides" which Applicants' have not addressed.

The Examiner notes the discussion above for Claims 29, 30, 57, 62, which have no broad structural feature, and how the structure defines the inherent function that is a real limitation on the claims, although not expressed.

More particular to Claim 32 is the immunological reactivity of the claimed polypeptide. As previously noted, "the instant specification fully describes polypeptide fragments of disclosed sequences which **can** interact with antibodies. However, the instant specification has not

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described ... polypeptide fragments which **would** interact with the noted antibodies.” (emphasis added). Although the genus of immunoreactive polypeptides specific for SEQ ID NO:20 over SEQ ID NO:2 is discussed in the specification, there is no evidence that any representative species of such a large and varied genus was in the possession of the inventors at the time of filing. To satisfy the written description aspect of 35 U.S.C. § 112, first paragraph, for a claimed genus of molecules, it must be clear that: (1) the identifying characteristics of the claimed molecules have been disclosed, e.g., structure, physical and/or chemical characteristics, functional characteristics when coupled with a known or disclosed correlation between function and structure, or a combination of these; and (2) a representative number of species within the genus must be disclosed. The specification does not disclose any representative species of any of the recited classes of possible immunoreactive polypeptides specific for SEQ ID NO:20 over SEQ ID NO:2, with or without identifying characteristics. Therefore, claim 32, as written, fails to satisfy the written description requirement.

44. Previous rejection of Claim 87 under 35 U.S.C. § 112, first paragraph, written description, is maintained. Applicants’ arguments have been fully considered but are not deemed persuasive. Applicants’ arguments discuss only the amendments. The amended claim also has written description issues as addressed below.

The Examiner notes the discussion above for Claims 29, 30, 57, and 62, which have no broad structural feature, wherein the structure defines the inherent function that is a real limitation on the claims, although not expressed.

***Withdrawn - Claim Rejections - 35 U.S.C. § 102***

45. Claims 10, 12, 13, 15-18, 28, and 87-89 are rejected under 35 U.S.C. 102(b) as being anticipated by Heim *et al.* is withdrawn by virtue of Applicants' amendment to Claims 10, 28, and 87 and the cancellation of Claims 88-89.

Claim 10 has been amended to read on a polypeptide comprising SEQ ID NO:2 modified in particular positions; the additional "30% identity" limitation further limits the flanking regions of the entire protein comprising the particularly modified SEQ ID NO:2. Due to this amendment, the polypeptide of Heim *et al.* no longer reads on the claimed polypeptide since differences, other than the denoted residues in SEQ ID NO:2, are found in the polypeptide of Heim *et al.* It is noteworthy that Applicants did **not** present this argument in traversal of the rejection. Attention is brought to Applicants of the altered scope of the instant claims as noted above. Claim 28, as amended, overcomes Heim *et al.* as prior art with the inclusion of the limitation of being 30% identical to SEQ ID NO:2; the protein of Heim *et al.* is only 26% identical. However, a new art rejection is set forth based on the amended Claim 28 (see below).

46. Previous rejection of Claim 29 under 35 U.S.C. § 102(b) as being anticipated by Clausen *et al.* is withdrawn by virtue of Applicants' amendment to said claim to include only "conservative substitutions" as defined in the specification on page 10. Alterations, such as K to E and K to Q are not considered conservative.

***Maintained - Claim Rejections - 35 U.S.C. § 102***

47. Previous rejection of Claim 9 under 35 U.S.C. § 102(b) as being anticipated by Kleber-Janke *et al.* is maintained. Applicants' arguments have been fully considered but are not deemed persuasive at this time.

Applicants' arguments concerning the priority date granted to Claim 9 cannot be confirmed by the Examiner at this time since 08/740,682, filed on November 1, 1996 (which the instant application is a continuation-in-part of), is currently unavailable in the publication division awaiting patenting. If Applicants' assessment that 08/740,682 discloses the invention in Claim 9 is concurred by the Examiner, the instant rejection will be withdrawn.

In addition to not being prior art, Applicants' argue that Kleber-Janke *et al.* do not discuss modifying the polypeptide and, therefore, cannot read on Claim 9. This is not the case. Whether the sequence of the polypeptide is naturally-occurring or whether it is obtained via modification, the polypeptide product is the SAME unless Applicants can demonstrate how the product obtained via modification is somehow different from the product obtained via natural sources.

48. Previous rejection of Claims 19 and 21 under 35 U.S.C. § 102(b) as being anticipated by Cordero *et al.* is maintained. Applicants' arguments have been fully considered but are not deemed persuasive. Applicants argue that Cordero *et al.* made no changes to the polypeptides, and this lack of modification sets the polypeptide of Cordero *et al.* apart from the claimed polypeptide. The Examiner disagrees. As noted above, the polypeptide product, regardless of how it was made, has a particular structure. If the limitations of this structure are met, all the limitations of the claims are met. If the modification process renders the polypeptide obtained via modification procedures different from a polypeptide obtained through procedures without modification, then the structure of the resulting product would be different according to the process made. This is not the case here.



The Examiner notes that the polypeptide of Cordero *et al.* is about 50% identical to SEQ ID NO:2, thus also meeting the amended limitation in the claims.

The Examiner further notes that if Claims 19 and 21 are amended to read ---A polypeptide comprising SEQ ID NO:2 modified to contain two or more modifications...---, the instant rejection would be obviated since the polypeptide of Cordero *et al.* does **not** match SEQ ID NO:2 in only the noted modification positions.

## NEW OBJECTIONS/REJECTIONS

### *Objections to the Specification*

49. The amendment filed December 31, 2001 is objected to under 35 U.S.C. § 132 because it introduces new matter into the disclosure. 35 U.S.C. § 132 states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows:

- a) In Claim 62, the inclusion of SEQ ID NOs: 35-53 as, previously stated, wild-type CI-2 polypeptides.
- b) In Claim 78, a polypeptide having at least 60% sequence identity to SEQ ID NO:4.
- c) In Claim 79, a polypeptide having at least 60% sequence identity to SEQ ID NO 6.
- d) In Claim 80, a polypeptide having at least 70% sequence identity to SEQ ID NO 6.
- e) In Claim 81, a polypeptide having at least 60% sequence identity to SEQ ID NO 8.
- f) In Claim 82, a polypeptide having at least 70% sequence identity to SEQ ID NO 8.
- g) In Claim 83, a polypeptide having at least 60% sequence identity to SEQ ID NO:10.
- h) In Claim 84, a polypeptide having at least 70% sequence identity to SEQ ID NO:10.
- i) In Claim 87, a polypeptide related to SEQ ID NOs: 24, 26, 28, 30, 32, or 35-53 and modified to contain a disulfide bond.

Concerning Claim 62, Applicants amended previously claimed "wild-type CI-2 polypeptides" to ---SEQ ID NOs: 2, 4, or 35-53---. Only SEQ ID NOs: 2 and 4 are noted as wild-type CI-2 polypeptides in Figures 1 and 2; all the other sequences are noted as homologs. Support for conservatively substituted variants of SEQ ID NOs: 35-53 is not cited.

Concerning Claims 78-84, Applicants note that the phrase "at least 60% sequence identity" or "at least 70% sequence identity" as related to SEQ ID NOs: 4, 6, 8, and 10 is supported by the disclosure in the specification on page 12 referring to "the modified protein". The Examiner finds no definition of "the modified protein" being exactly SEQ ID NOs: 4, 6, 8, or 10.

Concerning Claim 87, no reference to the species of SEQ ID NOs: 24, 26, 28, 30, 32, or 35-53 containing non-native disulfide bonds is cited. The Examiner can find no clear support.

Applicants are required to cancel the new matter in the reply to this Office Action or to point out **precisely** (page and line number) where in the instant application, or where in any incorporated-by-reference publications, clear support for the amendments can be found.

### *Claim Objections*

50. Claim 62 is objected to under 37 C.F.R. § 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. The additional breadth in Claim 62 to include "conservatively substituted variants" of Claim 61 does not further limit the subject matter of the parent claim.

***Claim Rejections - 35 U.S.C. § 112***

The following is a quotation of the second paragraph of 35 U.S.C. § 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

51. Claim 12 is rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The phrase "wild-type Cl-2" is unclear since, in Figure 1, both SEQ ID NOs: 2 and 4 are described as wild-type. Which wild-type sequence is intended as the reference here? Or do both sequences have identical inhibitory activities with the noted proteases?

52. Claim 14 is rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The transitional phrase should be ---further comprising--- and not "comprising" since the cysteine mutations added are not part of the possible mutations using essential amino acids in the parent claim 10. Without further comprising, the concept of cysteine as an essential amino acid is confusing.

53. Claim 18 is rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The word "about" is unclear in reference to "about eighteen additional residues". Specifically, this claims is drawn to adding an N-terminal extension onto the polypeptides wherein the extension corresponds to residues 1-18 of SEQ ID NOs:2 or 12. Does "about"

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indicate that 1-17 can be used? 1-15? 2-18? The metes and bounds of the word "about" is confusing.

54. Claim 32 is rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for the term "conservatively substituted". The citation in the specification on page 10 defining the term is unclear as noted above.

55. Claims 59, 61, 72, 74, 76, 78-84, and 87 and their dependent claims (Claims 60, 62-71, 73, 75, 77, 85, and 86) are rejected under 35 U.S.C. § 112, first paragraph, written description - new matter, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The new matter objections maintained and set forth above describe the lack of support for the instant claims in the specification as originally filed.

***Claim Rejections - 35 U.S.C. § 101***

35 U.S.C. § 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

56. Claims 29-32 and 58-59 are rejected under 35 U.S.C. § 101 because the claimed invention is directed to non-statutory subject matter. Claims 29-32 and 58 require no hand-of-man in the production of the claimed invention; polypeptides meeting the claim limitations can be naturally-occurring. Claim 59 reads on a product of nature wherein the hand-of-man was not

required to produce the claimed invention. The Examiner suggests inserting the term "isolated" before the claimed product in the preamble.

***Claim Rejections - 35 U.S.C. § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

57. Claim 28 is rejected under 35 U.S.C. § 102(b) as being anticipated by Cordero *et al.* The instant rejection is an extension of the rejection previously applied, and herein maintained, against Claims 19 and 21.

Cordero *et al.* teach a 73 amino acid polypeptide that is about 50% identical to SEQ ID NO:2 (see previously attached alignment). The following positions corresponding to SEQ ID NO:2 in the polypeptide of Cordero *et al.* are modified with respect to SEQ ID NO:2, using essential amino acids.

| <u>SEQ ID NO:2</u> | <u>Cordero <i>et al.</i></u> |
|--------------------|------------------------------|
| <b>Q41</b>         | <b>K34</b>                   |
| <b>I49</b>         | <b>V42</b>                   |
| (I56               | V49) excluded                |
| <b>M59</b>         | <b>A52</b>                   |
| <b>N75</b>         | <b>I65</b>                   |
| <b>I76</b>         | <b>V66</b>                   |
| <b>V79</b>         | <b>T69</b>                   |

The replacement residues, Lys, Val, Ala, Ile, and Thr are essential amino acids. Thus, the polypeptide of Cordero *et al.* contains 6 "substitutions" with respect to SEQ ID NO:2.

The Examiner notes that if Claim 28 was amended to read ---A polypeptide comprising SEQ ID NO:2 modified to contain three or more modifications...---, the instant rejection would be obviated since the polypeptide of Cordero *et al.* does **not** match SEQ ID NO:2 in only the noted modification positions.

58. Claim 59 is rejected under 35 U.S.C. § 102(b) as being anticipated by Williamson *et al.* (IDS Paper No. 14, reference #A29). The instant claim is drawn to a polypeptide having 60% identity with SEQ ID NO:2 and having at least 50 residues, at least eight of which are lysine residues.

Williamson *et al.* teach the wild-type high-lysine barley chymotrypsin inhibitor-2 (CI-2); this sequence is identical to SEQ ID NO:2, 84 amino acids long, and has 8 lysine residues.

### *Summary of Issues Pending*

59. The following is a summary of the issues pending in the instant application.

- a) Compliance with the sequence rules.
- b) The specification stands objected to for having an incomplete Abstract.
- c) The specification stands objected to for containing new matter:
  - 1) In Claim 59 (e), the phrase "at least 60% sequence identity ... SEQ ID NO:2"
  - 2) In Claims 61, 72, 74, and 76 to references to SEQ ID NO:2, positions "19-53 and 70-83" and "19-83".
  - 3) In Claim 62, the inclusion of SEQ ID NOs: 35-53 as, previously stated, wild-type CI-2 polypeptides.
  - 4) In Claim 78, a polypeptide having at least 60% sequence identity to SEQ ID NO:4.
  - 5) In Claim 79, a polypeptide having at least 60% sequence identity to SEQ ID NO:6.

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- 6) In Claim 80, a polypeptide having at least 70% sequence identity to SEQ ID NO:6.
- 7) In Claim 81, a polypeptide having at least 60% sequence identity to SEQ ID NO:8.
- 8) In Claim 82, a polypeptide having at least 70% sequence identity to SEQ ID NO:8.
- 9) In Claim 83, a polypeptide having at least 60% sequence identity to SEQ ID NO:10.
- 10) In Claim 84, a polypeptide having at least 70% sequence identity to SEQ ID NO:10.
- 11) In Claim 87, a polypeptide related to SEQ ID NOs: 24, 26, 28, 30, 32, or 35-53 and modified to contain a disulfide bond.

- d) Claim 62 stands objected to under 37 C.F.R. § 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim.
- e) Claim 12 stands rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for the phrase "wild-type CI-2".
- f) Claim 14 stands rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for lacking the transitional phrase ---further comprising---.
- g) Claim 18 stands rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for the word "about".
- h) Claims 29, 32, and 62 stand rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for the term "conservatively substituted".
- i) Claims 29, 30, 32, 57, 62, and 87 stand rejected under 35 U.S.C. § 112, first paragraph, written description.
- j) Claims 59-87 are rejected under 35 U.S.C. § 112, first paragraph, written description - new matter.
- k) Claims 29-32 and 58-59 stands rejected under 35 U.S.C. § 101 because the claimed invention is directed to non-statutory subject matter.
- l) Claim 9 stands rejected under 35 U.S.C. § 102(b) as being anticipated by Kleber-Janke *et al.*

- m) Claims 19, 21, and 28 stand rejected under 35 U.S.C. § 102(b) as being anticipated by Cordero *et al.*
- n) Claim 59 stands rejected under 35 U.S.C. § 102(b) as being anticipated by Williamson *et al.*

### *Conclusion*

60. Claims 9, 12, 14, 18, 19, 21, 28, 29-32, 57-87 are rejected. Claims 22-25, 54-55, and 97 are objected to for depending from a rejected claim. Claims 10, 11, 13, 15-17, 20, 56, and 96 are allowed. Applicants must respond to the objections/rejections in each of the numbered sections in this Office action to be fully responsive in prosecution.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See M.P.E.P. § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. § 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 C.F.R. § 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.



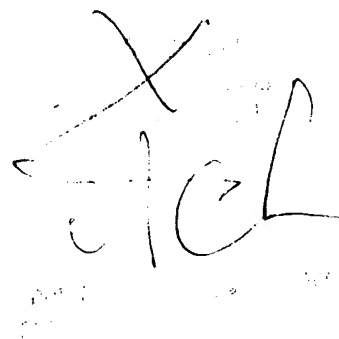
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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kathleen M Kerr whose telephone number is (703) 305-1229.

The examiner can normally be reached on Monday through Friday, from 8:30am to 5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathupura Achutamurthy can be reached on (703) 308-3804. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-0294 for regular communications and (703) 305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Handwritten signature and initials, possibly "KMK" or "KMKL", with a large "X" mark above them.

KMK  
May 1, 2002